TITLE: **HbA1c Testing Frequency: A Review of the Clinical Evidence and Guidelines**

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CONTEXT AND POLICY ISSUES

Estimates indicate that diabetes is one of the fastest growing chronic diseases affecting the world's population.[1,2] In 2011 it was calculated that there were approximately 366 million people affected by this disease worldwide and this number has been projected to reach 500 million by the year 2030.[1,3] This is a potential increase of close to 50% in only 19 years. In Ontario the prevalence of diabetes is on the rise. Assessments have demonstrated that the prevalence of type II diabetes was 800,000 between 2011 and 2012.[3]

Clinical testing is an essential part of the health care process and is utilized primarily to give insight into a patient's condition.[4] In addition, testing will indicate what choices a physician should make in order to benefit a patient and help to modify their therapy in response to fluctuating disease states. In diabetes diagnosis and monitoring one of the primary tests conducted is a hemoglobin A1c, or HbA1c, test. This is a measure of β-N-(1-deoxy)-fructosyl hemoglobin contained within the red blood cell which is glycated in varying amounts depending on blood glucose levels over time.[5] This protein is found within the red blood cell for its entire life span of approximately 120 days.[3,5,6] For diagnosis and monitoring, HbA1c analysis is much easier for a patient to complete than other methods of blood glucose testing as no prolonged period of dietary restriction is required. Additionally, it is completed rapidly, requiring only a sample of blood as opposed to an oral glucose tolerance test which requires a strict diet three days prior to testing and a two hour absorption time after ingestion of a measured amount of glucose.[6] In addition HbA1c testing has no overt requirement from the patient and is not dependent on any sort of prandial status which means that it may be taken at any time day or night. Finally, glucose testing must be sent to the laboratory for measurement within thirty to sixty minutes from the time it was sampled. This is due to the red blood cells continuing to metabolize glucose post-withdrawal at a rate of 7% per hour.[6] The protein analyzed in HbA1c testing is capable of remaining stable for over a week if kept refrigerated.

With the dramatic rise in the prevalence of diabetes comes an associated increase in the amount of HbA1c testing that is required. Current estimates indicate that there is an average annual increase of 8-10% in workload in medical laboratories.[7] In Ontario during 2011 and

2012, the total number of HbA1c tests completed was 3.4 million with an associated cost of $30 million dollars.[3,8] This is an increase of 55% from 2007-2006 where a total of 2.2 million tests were completed.[3] During the same period 1.4 million HbA1c tests were conducted in non-diabetic patients.[3] It has been estimated that the health related expenditures for patients with diabetes are at least 2.4 times higher than those for non-diabetic patients.[9] This brings to the forefront the need to determine an optimal frequency for HbA1c testing in order to manage both healthcare budgets and productivity.

While published guidelines have described treatment goals and give minimum limits for testing frequency there is a lack of defining criteria for the maximum number of tests or the optimal testing frequency for ideal control.[10,11] In addition to this problem, previous studies demonstrate that testing is used in patients who do not require it, such as in those who are not diabetic, and those who have had no history of problems with glycemic control.[8,10] HbA1c testing is typically done twice yearly in well controlled patients and four times yearly in poorly controlled individuals.[3,11,12] Studies have shown that both over and under-utilization trends are commonplace in clinical practice.[10] For example it has been found that some individual patients have received a total of 28 HbA1c tests in a single year.[10] The reverse of this has also been found where individual patients are only tested one time in a two year long period.[10]

The purpose of this report is to examine the evidence on the effect of different testing frequencies for HbA1c and discuss the guidelines governing the timing of use.

RESEARCH QUESTIONS

1. What is the clinical evidence regarding different HbA1c testing frequencies for patients with type 1 or type 2 diabetes?

2. What are the evidence-based guidelines regarding HbA1c testing frequency for patients with type 1 or type 2 diabetes?

KEY FINDINGS

Although there was the suggestion of potential benefit to shortened HbA1c testing intervals for some patients in non-randomized studies, evidence from a randomized controlled trial indicated that clinical outcomes for well-controlled patients tested at 3- or 6-month intervals were equivalent. Studies demonstrated that adherence to guidelines was able to improve variations in HbA1c levels. Clinical practice guidelines generally agree that HbA1c testing every six months is appropriate for patients who are well controlled. For those patients that have poorly controlled diabetes or who are making changes in their therapeutic regimen a testing once every three months was advised.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2014, Issue 8), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. Where possible,

retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2009 and August 28, 2014.

Rapid Response reports are organized so that the evidence for each research question is presented separately

Selection Criteria and Methods

One reviewer screened the titles and abstracts of the retrieved publications and evaluated the full-text publications for the final article selection based on the criteria outlined in Table 1.

Table 1: Selection Criteria

Population	Patients with diabetes
Intervention	HbA1c testing
Comparator	Different testing frequencies
Outcomes	Clinical effectiveness (e.g. improved glycemic control) Guidelines
Study Designs	HTA/ Systematic review/Meta-analysis, Non-randomized studies, Randomized controlled trials, Evidence-based Guidelines

Exclusion Criteria

Articles and guidelines were excluded from this report if they did not meet the criteria detailed in Table 1, were included in a selected systemic review, or were published prior to January 1, 2009.

Critical Appraisal of Individual Studies

Systemic reviews were assessed using the Assessment of Multiple Systemic Reviews (AMSTAR) tool.[13] Randomized controlled trials and non-randomized studies were assessed using the Downs and Black checklist for the adequacy of allocation concealment, blinding of patients, healthcare providers, clinicians, data collectors and outcome assessors, randomization, losses to follow-up, description of intention-to-treat, and early stopping of trial.[14] Guidelines were assessed using the Appraisal of Guidelines for Research and Evaluation II.[15]

SUMMARY OF EVIDENCE

Quantity of Research Available

The literature search identified 255 citations for review. After examination of titles and abstracts, 236 were rejected and 19 were retrieved for full text screening. Five additional studies were identified in the grey literature or by hand searching. Of these, 19 did not meet the inclusion criteria and were excluded. In total, five publications were selected for inclusion. These publications included one rapid systematic review of clinical practice guidelines, one randomized controlled trial, and three non-randomized studies. No health technology

assessments or meta-analyses were identified for inclusion. The study selection process is outlined in a PRISMA flow chart in Appendix 1.

Summary of Study Characteristics

Detailed characteristics for all of the included investigations can be found in Appendix 2.

Clinical evidence regarding different HbA1c testing frequencies for patients with diabetes

One randomized controlled trial was identified for the question posed in this report.[3] It was produced in 2014 in The Netherlands and examined results obtained between April 2009 and August 2010. It included 791 type II diabetics from 233 general practitioners across the country. The goal was to determine the effectiveness and the cost-effectiveness of either 3-monthly (control) or 6-monthly (intervention) monitoring of well-controlled diabetics. Well controlled was defined as patients with HbA1c ≤58 mmol/mol, systolic blood pressure ≤145 mmHg and total cholesterol ≤5.2 mmol/L. These patients were randomized into either the control or intervention group and followed up for eighteen months. The primary outcome of interest was the percentage of the population of either group that maintained well-controlled results. Equivalence between groupings was assumed when two-sided 95% confidence intervals fell between -5% and 5%. Secondary outcomes were also examined and included body mass index, smoking, diabetic related stress, and the perceived level of hypo- or hyper-glycemic events.

There were three non-randomized studies found that examined different testing frequencies for HbA1c testing in patients with diabetes. The first of these investigations was produced in The National University Hospital Singapore and examined 9,173 patients who had a total of 26,026 HbA1c tests performed during the 2006 to 2007 fiscal year.[16] It utilized a retrospective cross-sectional procedure to examine the proportion of HbA1c testing that was different enough from previous results to elicit changes in clinical decisions when completed at different testing intervals in medical practice. The study was not limited to a specific diabetes type and the average age of the participants was 60 years old. Patients must have had more than a single HbA1c test conducted within the time period of the study.

The remaining two studies were both produced in the United States of America and used retrospective cohort analyses to obtain their goals. The first of these investigations was conducted using medical records from hospitals in New York and Pennsylvania.[12] It examined 193 patients with type II diabetes to determine if patients who followed published guidelines had better glycemic control than those who did not. Patients were excluded if they were deceased, had gestational diabetes, had type I diabetes, had no HbA1c testing, had only POC testing, or were anemic. The final study was based on medical records from several regions of Florida, Pennsylvania, and Delaware.[17] The goal was to determine the association between HbA1c testing frequency and clinic visits against glycemic control in youth with type I diabetes. They examined 1,449 patient records of people with an average age of 11.4 years and were tested between July 2008 and June 2011. All patients must have had a diagnosis of type I diabetes prior to the start of the study and visited one of the five clinics in the first half of 2008. They were excluded if they had only one visit during the study period or were treated for less than one year.

Evidence-based guidelines regarding HbA1c testing frequency

The rapid systematic review included in this report was produced in Ontario, Canada by the Evidence Development and Standards Branch at Health Quality Ontario in 2014.[8] The search was limited to include systematic reviews, health technology assessments and meta-analyses published between January 1, 2008 and May 2, 2013. The literature search produced 1,654 results of which one health technology assessment and six clinical practice guidelines (CPGs) were appropriate for inclusion. The health technology assessment contained an analysis of three evidence based guidelines; the National Institute for Health and Care Excellence (NICE) guidelines produced in 2009, the Canadian Diabetes Association guidelines produced in 2008 and the International Diabetes Federation guidelines produced in 2005. The six CPGs were authored by: the Canadian Diabetes Association in 2013, the American Diabetes Association in 2011, the American Association of Clinical Endocrinologists in 2011, Diabetes Australia in 2009, NICE in 2009, and the Society for Endocrinology Metabolism and Diabetes of South Africa in 2012.

Summary of Critical Appraisal

Details of the critical appraisal of individual studies can be found in Appendix 3.

Clinical evidence regarding different HbA1c testing frequencies for patients with diabetes

The randomized controlled trial found for this question provided a set of easily generalizable results due to the large amount of included general practitioners used in the investigation.[3] It also contained well detailed explanations of all included methodologies including techniques for patient randomization. During the study period there was no method to keep patients blinded to results such as blood pressure or weight. This may result in some of the clinical outcomes of interest such as stress and physical activity. Additionally, in order to determine any long term trends, an eighteen month trial period may not be substantial enough as all included patients were already well-controlled. The patient population was drawn from a larger group with participants being given a choice of which testing frequency to receive based on preference. The remaining participants who did not express a preference were included in this study, and it is unclear how this method of patient selection may affect generalizability. The authors state that the testing of HbA1c and cholesterol was not at exactly baseline or 18 month intervals but failed to show the deviation trends in their figures. Finally, the authors reported a lower success rate in meeting clinical targets than expected; therefore the study was underpowered to formally demonstrate equivalence as a larger sample size was required.

The three non-randomized studies examined in this report all employed a retrospective cohort analysis. As a result of this they are all subject to the inherent limitations of this type of study, such as the lack of randomization leading to potential selection bias and the potential for detection bias. The study produced by Parcero et al was also restricted by including a majority of Caucasian patients meaning that it will not be generalizable to all populations.[12] In the examination by Loh et al the cross-sectional study design resulted in testing intervals that are not randomized which may result in data that does not represent the actual longitudinal trends.[16] The study by Phan et al. was unable to control for factors that had the potential to influence glucose levels, such as the duration of insulin use and the duration of diabetes diagnosis, as well as factors which may impart bias to clinic visit frequency, such as provider preference and patient motivation.

Evidence-based guidelines regarding HbA1c testing frequency

The rapid systematic review found for this question contained well defined criteria for literature inclusion or exclusion and had well documented descriptions of all parties contributing to review development. The literature search was limited to health technology assessments, systematic reviews, meta-analyses and clinical practice guidelines. Furthermore the search was limited to a five-year period ending 2013. The limitations to search timeframe and eligible study designs increase the possibility that relevant literature was not captured. Study selection was conducted by a single reviewer. The target populations for both readers and patients are described in detail. However, a limited amount of discussion was provided for each question being examined. There was also a lack of any discussion of the limitations, strengths, or amount of supporting evidence for the guidelines included in the review.

Summary of Findings

Details for all of the investigations discussed in this section may be found in Appendix 4.

Clinical evidence regarding different HbA1c testing frequencies for patients with diabetes

The randomized controlled trial included here investigated the effectiveness and cost-effectiveness for the use of 6-monthly monitoring (intervention) compared to 3-monthly monitoring (control) in well controlled type II diabetics.[3] Of the study population 69.5% of controls and 69.8% of intervention groups maintained well-controlled diabetes. The results for HbA1c level, blood pressure and cholesterol were equivalent for both groups. In addition, all of the secondary outcomes except for physical activity and the use of antihypertensive drugs were equivalent. Blood pressure was found to be beyond the equivalence boundaries though this was attributed to changes in the antihypertension drug regimen during the trial.

Loh et al.[16] examined different testing frequencies and how the results of HbA1c testing would influence clinical decisions. They found that out of the total population, 9% of tests were completed in less than 30 days and 42% in less than 90 days. Of these repeated tests, 27% had significant enough variation to cause the physician to alter their treatment strategy. When significantly changed HbA1c level is plotted against testing interval there is a clear linear trend up until a plateau is reached. This plateau represents the level where $P > 0.05$ and occurs where there is no longer any significant change in the proportion of patients with significant HbA1c changes. It occurs at an interval of 4 weeks in patients with an HbA1c level of >8% indicating that shortened intervals may benefit certain patients. Well-controlled patients, HbA1c <7%, had no significant change at any timing interval.

The investigation by Parcero et al.[12] examined whether diabetic patients who adhered to guidelines for HbA1c testing would have better glycemic control than those who did not. They discovered that 51% of patients were following the guidelines, and that this percentage is made up mostly of well-controlled diabetics. The median HbA1c values in this group were significantly lower than those who went against the recommendations. By the use of univariate analysis a significant association was detected between glucose control and adherence to guidelines. These findings were somewhat replicated in the study by Phan et al. where quarterly visits and HbA1c testing led to the most stable HbA1c levels in the testing group.[17] It was also found that the average patient visit to clinics was 3.2 per year.

Evidence based guidelines regarding HbA1c testing frequency

The systematic review included here documented findings from one health technology assessment (reporting on three guidelines) and six additional clinical practice guidelines. The results from all included literature demonstrated that an HbA1c testing frequency of once every three months is appropriate for patients who have poorly controlled diabetes or who are making changes in their therapeutic regimen. In patients who are well controlled a testing interval of once every six months is advised. It was also found that at no time should HbA1c testing be completed more than four times in a single year. These recommendations are applicable to both type I and II diabetic patients.

Limitations

The systematic review included here was well written and contained details for target populations and provided a concise overview of the issues of HbA1c testing frequency. It was limited by a lack of detail for each of the proposed questions under examination. Additionally it suffered from a lack of any discussion of limitations, strengths or amount of included supporting evidence for the included guidelines. The randomized controlled trial utilized here obtained a high rate of participation from a wide variety of locations and as a result is easily generalizable to a wide selection of the population. Unfortunately the study follow-up may not be long enough to achieve the desired outcome. Additional outcomes such as diabetes-related stress and physical activity may be affected by bias from an inability to keep patients blinded to these results during routine clinic visits. The non-randomized studies all used retrospective cohort analyses whereby data is collected from past medical records. These studies are all subject to potential bias through selection criteria and the fact that all information gathered at the time of patient clinic visit was collected by individuals that were not part of the current study therefore it is not possible to control for exposure or outcome assessment.

Recommendations regarding HbA1c testing frequency were developed using information produced primarily from expert consensus and clinical experience not from scientific study as evidence to inform recommendations is limited.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

The question regarding different HbA1c testing frequencies for diabetes patients remains elusive and there is evidence of inappropriate HbA1c testing of both over- and under-use.[7,10] There tends to be an overall lack of adherence to published guidelines in all regions that were examined. This problem is partially explained by the fact that the guidelines only describe the minimum amount of testing and make no mention of a maximum limit. There are conflicting results for the benefit of shortened testing intervals however one randomized controlled trial found that clinical outcomes were equivalent for patients testing every 3 months or every 6 months.

Evidence-based guidelines were in general agreement that an HbA1c testing frequency of once every six months is appropriate for patients who are well controlled. For those patients that have poorly controlled diabetes or who are making changes in their therapeutic regimen a testing interval of once every three months was advised.

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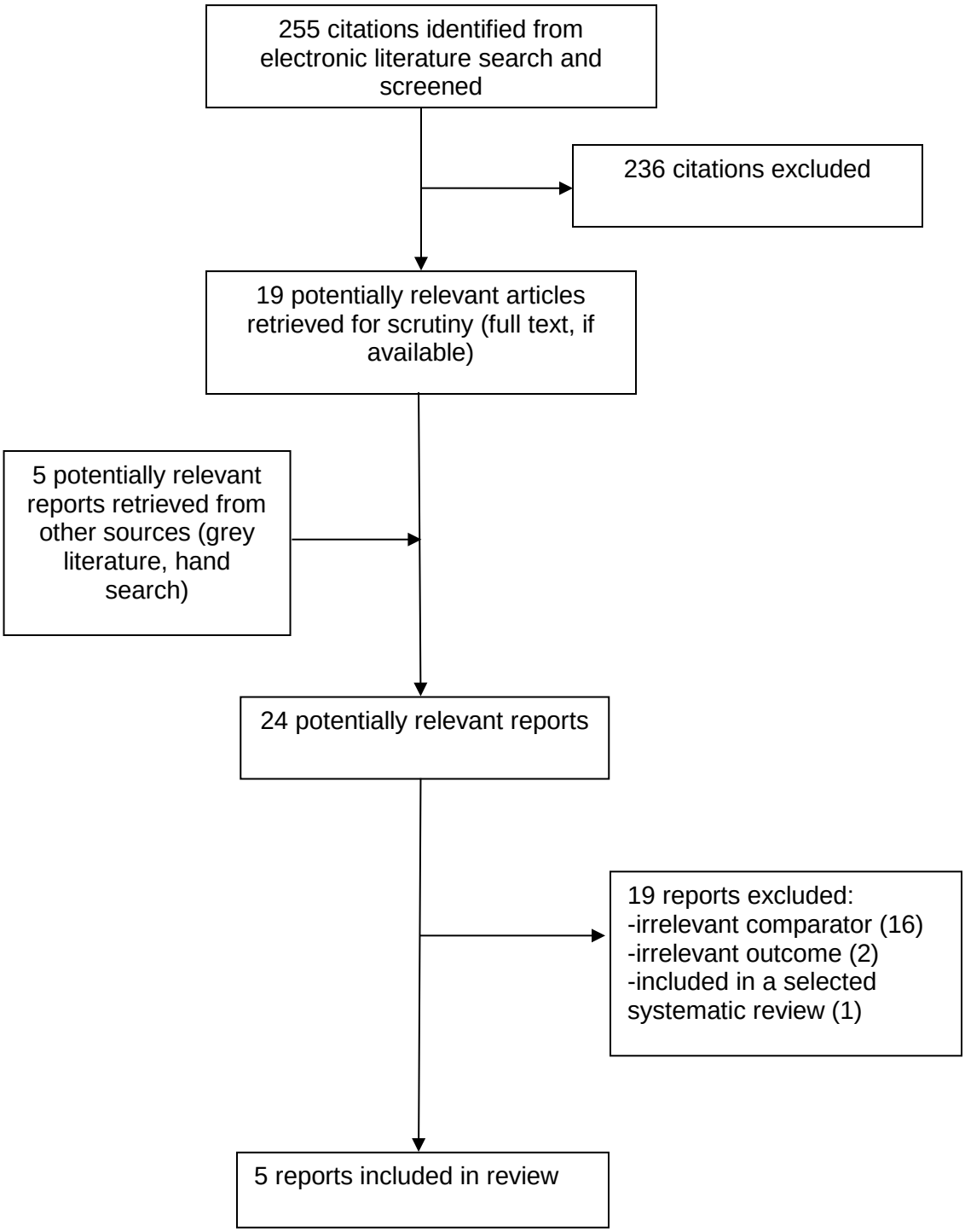
APPENDIX 1: Selection of Included Studies



APPENDIX 2: Summary of Study Characteristics

First Author, Publication Year, Country	Eligibility Criteria	Included Study Designs / Overall Goals	Number of Included Studies
Systematic Reviews			
Health Quality Ontario, 2014, Canada[8]	• Investigation completed by the Evidence Development and Standards branch of Health Quality Ontario • Expert Advisory Panel on Community-Based Care for Adult Patients with Type II Diabetes was made up of physicians, nurses, dietitians, community representatives and officials from the Ministry of Health and Long-Term Care in Ontario • Literature published in English language between January 1 2008 to May 2 2013	• Literature search completed using Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid, Embase, EBSCO Cumulative Index to Nursing and Allied Health Literature (CINAHL), the Wiley Cochrane Library, and the Centre for Reviews and Dissemination database	Seven publications included

First Author, Publication Year, Country	Study Design, Basic Methodology	Population Characteristics, Sample Size (n)	Goal
Randomized Controlled Trials			
Wermeling et al, 2014, The Netherlands [3]	• Study took place between April 2009 and August 2010 • Upon trial initiation patients asked if they prefer 3 or 6 month interval for testing, if strong opinions encountered then these patients were excluded if not then were randomized to either grouping. (n=791patients seen by 233 different GP's) • Randomized to either 3 month (control) or 6 month (intervention) group using a 1:1 ratio and processed using a computerized random number generator • Randomization completed at	• patients must have diagnosis of type II diabetes for at least 1 year, be between 40-80 years old, obtain treatment from a GP, not receiving insulin treatment, be well-controlled (have an HbA1c ≤ 58 mmol/mol, have systolic blood pressure ≤ 145 mmHg and total cholesterol ≤ 5.2mmol/L)	To determine the effectiveness and cost-effectiveness of 6-monthly monitoring compared with 3-monthly monitoring of well-controlled type II diabetic patients utilizing primary care facilities

First Author, Publication Year, Country	Study Design, Basic Methodology	Population Characteristics, Sample Size (n)	Goal
	the patient level. Laboratory technicians at the analysis centers were also blinded to the groupings. • Primary results are the percentages of patients able to maintain well-controlled diabetes • Secondary goals are separate targets for: - HbA1c, systolic BP[2], total cholesterol (all completed on a continuous scale) - Body mass index - Results of a questionnaire given out at baseline and after 18 months on: smoking, physical activity, health status (SF-36 and EQ-5D), diabetes-related stress, satisfaction with treatment, perceived frequency of hypo- or hyperglycaemias, and medication use • Equivalence between control and intervention groups is assumed when two-sided 95% confidence Intervals fall between -5% and 5%	• n=791, 397 in 6 month group and 394 in 3 month group	
Non-Randomized Studies			
Loh et al., 2011, Singapore[16]	• Retrospective cross-sectional analysis • Conducted in The National University Hospital Singapore on patients examined during 2006 and 2007 • Use NGSP level 1 certified testing • The critical difference is the minimum change required before two consecutive results are considered different enough	• Include patients if they were tested for HbA1c more than one time during study period • N=9173 patients and 26,026 HbA1c tests • Mean patient age is 60 years old	To examine the proportion of HbA1c testing that had revealed changes different enough to influence clinical decisions when repeated at different testing intervals in clinical practice

First Author, Publication Year, Country	Study Design, Basic Methodology	Population Characteristics, Sample Size (n)	Goal
	to cause a clinical decision to be changed		
Parcero et al., 2011, United States of America[12]	• Retrospective case report • Examine patients seen between January 1 2009 and June 30 2009 in the twin tiers region of New York and Pennsylvania • Review medical records and those with HbA1c results <7% considered controlled, ≥7% considered uncontrolled • Determined to be following guidelines on frequency if an HbA1c result of <7% was followed by test 6 months after or if result ≥7% followed by test 3 to 4 months after • Record type of therapy, gender and age as well	• Type II diabetics only • N=193 • Exclude patients if deceased, had gestational diabetes, had type I diabetes, had no HbA1c or only POC testing or had anemia	To test the premise that patients adhering to guidelines for HbA1c testing frequency have better glycemic control
Phan et al., 2014, United States of America[17]	• Retrospective cohort study • Medical records extracted from July 2008 to June 2011 • Study region was Jacksonville, Orlando, Pensacola in Florida or Philadelphia Pennsylvania or Wilmington Delaware • Criteria such as age, race, sex, clinic location and insurance status were recorded • POC used for testing method • Hierarchal cluster analysis used to analyse variables such as baseline characteristics, demographics clinic visits and testing frequency	• Patients included if seen at any of the five Nemours paediatric endocrinology clinics during the first half of 2008 and had an existing diabetes type I diagnosis • Excluded if only 1 visit, had only one HbA1c test or were treated for <1 year • N=1449 and mean age 11.4 years	To evaluate the association between the frequency of visits and glycated haemoglobin measurements on glycemic control in youth with type I diabetes

BP – blood pressure; GP - general practitioner; NGSP – National Glycohemoglobin Standardization Program; POC – Point of care

APPENDIX 3: Critical Appraisal of Included Literature

First Author, Publication Year	Strengths	Limitations
Systematic Reviews		
Health Quality Ontario, 2014[8]	• Contained a clearly defined method for paper inclusion and detailed what reference libraries were searched • Clearly listed all members of the Expert Advisory Panel and gave descriptions of their backgrounds • Gave clear description of target patient population and for applicability and the target audience that will benefit from reading the review	• A limited amount of detail was given for each question under examination. • Further discussion of the guidelines in aspects such as limitations, strengths and amount of included supporting evidence would be of benefit
Randomized Controlled Trials		
Wermeling et al., 2014[3]	• Is readily generalizable as the large number of included clinics represent all factors of the population • Well detailed explanation of all included methodologies used including patient randomization into 3 or 6 month groupings • Laboratory technicians were blinded to the randomization of all patients	• During the study period the testing for blood pressure or weight were known to the patient which may therefore impart bias to factors such as stress and physical activity • In order to determine long term trends an 18 month trial period may not be long enough to determine success or failure of an altered testing regimen when included patients are already well-controlled • Authors state that HbA1c and cholesterol testing was not measured at exactly baseline or 18 month intervals though the amount of deviation is not defined
Non-Randomized Studies		
Loh et al., 2011[16]	• Suitable statistical investigation was utilized • Appropriate caution is given when results are being discussed	• Cross-sectional study design means testing intervals are not randomized and therefore the data do not represent longitudinal trends • The conclusions reached here are all hypotheses as no benefit has been examined therefore the actual effect of shortened interval remains elusive
Parcero et al., 2011[12]	• All statistical techniques used are appropriate and are standard techniques for these	• Patients who missed an appointment during the 6 month follow up were not removed which therefore may cause

First Author, Publication Year	Strengths	Limitations
	inquiries • The results found in this investigation correlate with those of other studies	overestimation in results such as adherence rate • There is a very limited sample population which is mainly Caucasian making the interpretation of these results very specific
Phan et al., 2014[17]	• Excellent use of standardized statistical techniques found on other similar studies • Selected a wide variety of testing locations allowing for complete avoidance of bias for specific populations	• There is no method for accounting for factors such as duration of insulin dependence, insulin type used or duration of diabetes diagnosis • Specific factors that may affect glucose levels were not controlled for such as; interventions differing from meeting with physician/nurse in an endocrinology clinic and what device was used for HbA1c testing (POC of an external lab) • Factors that affect visit frequency such as provider preference and patient motivation/desire for improvement were not accounted for

APPENDIX 4: Summary of Findings

First Author, Publication Year	Main Study Findings	Author Conclusions
Systematic Reviews		
Health Quality Ontario, 2014[8]	• The Health Technology Assessment that was reviewed included discussion of three Evidence Based Guidelines: - National Institute for Health and Clinical Excellence 2009 - Canadian Diabetes Association 2008 - International Diabetes Federation 2005 All guidelines indicated that HbA1c testing once every three months is appropriate for patients who are receiving changes to their treatment regimen and those with poorly controlled glucose levels. If glycemic control is steady and meets treatment goals then testing every six months is acceptable. • The six Clinical Practice Guidelines that were reviewed were produced by: - The Canadian Diabetes Association 2013 - The American Diabetes Association 2013 - The American Association of Clinical Endocrinologists 2011 - National Institute for Health and Clinical Excellence 2009 - The Society for Endocrinology Metabolism and Diabetes of South Africa 2012 - Diabetes Australia 2009 All of these guidelines found that HbA1c testing once every three months is appropriate for patients not meeting treatment goals of those who require treatment regimen changes. Those with stable blood glucose results should be tested once every six months	• HbA1c has risen dramatically in Ontario since 2007 • When a patient's blood glucose levels are maintained as a stable level that reaches treatment goals HbA1c testing should be completed once every six months • When treatment goals are not being met and instability is encountered or when treatment regimens are being adjusted testing frequency of once every three months is recommended • At no time should more than four HbA1c tests be completed in a single year • All of the results found from these guidelines are applicable to both type I and II diabetics

First Author, Publication Year	Main Study Findings	Author Conclusions
Randomized Controlled Trials		
Wermeling et al., 2014[3]	• 69.5% of the control group maintained well-controlled diabetes compared to 69.8% of the intervention group though this found to be not equivalent (95% CI -6.2% to 6.7%, difference is 0.3%) • HbA1c, systolic BP and total cholesterol were equivalent in both groups • All secondary outcomes aside from physical activity and antihypertensive drug use were equivalent for both groups • Physical activity 95% CI -5.0% to 7.0% and antihypertensive drug use ±95% CI -0.3% to 5.4% • BP was found to be outside of equivalence range between groupings though attributed to alteration in antihypertensive drug regimen during trial. When these patients were removed achieved 78.6% of control group and 79.6% of intervention group maintained well-controlled status	• Patients with well-controlled type II diabetes and good cardiometabolic testing results are able to be seen by their physician less than four times per year • 6-monthly monitoring is not a strictly regimented interval and appropriate frequency must be assessed on a per patient basis • Guidelines should be modified to include a six monthly monitoring frequency as an option for well-controlled type II diabetics
Non-Randomized Studies		
Loh et al., 2011[16]	• 9% of retesting completed in under 30 days and 42% completed in under 90 days • 27% of repeat testing had significant changes and of this 12% occurred in <30 days and 26% occurred at less than 90 days • If plot the proportion of significantly changed HbA1c against testing interval is a clear linear rise until a plateau is reached • Plateau is where p=>0.05 between successive testing intervals and is reached by 4 week interval in patients with an HbA1c level of >8% (poor control group) • In patients with previous HbA1c at <7% (well controlled) was no significant change at any successive	• Noncompliance with guidelines for HbA1c testing intervals is commonplace • Several previous studies have indicated that shortened testing intervals are inappropriate but authors here conclude that this may not be true as significant changes in HbA1c levels can occur in specific populations with testing every 30 days or less • The high proportions of poorly controlled patients that had significant changes in under three months may have similar diagnostic yield as that according to guidelines • Is important to only use a shortened interval in patients who

First Author, Publication Year	Main Study Findings	Author Conclusions
	interval • Well controlled patients had lower proportion of significant changes than poorly (16% vs 44% respectively, p=<0.0001)	need it and an interval of no less than 4 weeks should be implemented
Parcero et al., 2011[12]	• 98 patients (51%) met frequency guidelines and 84 were well controlled HbA1c <7% • 95 did not meet frequency guidelines (49%) and 65 of these were poorly controlled • Median HbA1c values for patients adhering to guidelines were significantly lower than those not adhering (P<0.001) • 58% of those adhering to guidelines had HbA1c levels with good control (95% CI 51%-65%) • No significant difference found between male and female ratios for adherence to non-adherence groups (0.81 and 0.86 respectively) • Univariate analysis showed highly significant association between control of HbA1c and adherence to guidelines (OR13 95% CI 6.4-26.5; P<0.001) • OR for intensity of therapy and diabetes control is negatively associated (0.62 95% CI 0.51-0.75; P<0.001) • Age is positively associated with control though this correlation is weak OR=1.03 (95% CI 1.001-1.050; P=0.04) • Multiple logistic regression and both forward and backward stepwise regression demonstrate that only adherence to guidelines and intensity of therapy are independent correlates of control: Adherence OR: 15.3 95% CI 6.8-34.5 P<0.001 to guides Age OR: 1.027 95% CI: 0.996-1.059	• Results demonstrate that patients who adhere to guidelines maintain better glycemic control than those who do not • This finding is independent of variables such as age, gender or therapeutic intensity • Since only 51% of the population investigated here were adherent to guidelines a concerted effort to educate patients should be instituted

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	NS Therapy OR: 0.56 95% CI: 0.43-0.72 P<0.001 Gender OR: 0.58 95% CI 0.27-1.25 NS	
Phan et al., 2014[17]	• Mean HbA1c stayed almost stable over the course of the study, 8.3% (SD 1.5%) in first study year to 8.5% (SD 1.4%) in final year • 237 patients had HbA1c that worsened and 842 were stable and 370 improved over the course of the study • Those patients with higher baseline HbA1c were more likely to have improved control (F=1.43 p<0.001) • Average patient visits per year is 3.2 (SD 1.1) • Patients with 4 visits per year were the least likely to have worsened glycemic control (OR 0.36, p<0.001) and were most likely to have improved control (OR 3.48, p<0.001) • Multivariable regression analysis of race, insurance status and initial age had significant effects on visit frequency (p <0.005, <0.01 and <0.05 respectively) • Average tests per year is 3.0 (SD 1.0) and there were 2.8 (SD 0.7) fiscal quarters per year with a test • Those with 4 tests per year were least likely to have worsened control (OR 0.53 p<0.05) • Patients with more than 5 tests per year were the least likely to have improved control (OR 0.28 p<0.001) • Race, insurance status and initial age had significant influence on the frequency of HbA1c testing (p<0.01, <0.05 and <0.05 respectively) • Small number of patients had 5 or more visits per year and were more likely to have higher initial HbA1c (F=1.15 p<0.05), have Medicade (OR 2.13 P<0.001) and less likely to	• Quarterly visits and HbA1c testing may have the effect of alleviating the worsening of glycemic control in children with type I diabetes • Partial explanation for this is that those who have less frequent visits will miss important educational experiences • The grouping with 5 or more visits per year and worse control are likely those in need of more care as their glycemic control was suboptimal

First Author, Publication Year	Main Study Findings	Author Conclusions
	have improved glycemic control (OR 0.31 p<0.001)	

BP – blood pressure; CI – confidence interval; NS – Not significant; OR – Odds Ratio; SD – Standard Deviation